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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,928	10/13/2006	Bruce Joseph Roser	TOPT0103PUSA	6692
28395 7590 12/03/2009 BROOKS KUSHMAN P.C./FGTL 1000 TOWN CENTER 22ND FLOOR SOUTHFIELD, MI 48075-1238			EXAMINER HEYER, DENNIS	
			ART UNIT 1628	PAPER NUMBER
			MAIL DATE 12/03/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,928	ROSER, BRUCE JOSEPH	
	Examiner	Art Unit	
	DENNIS HEYER	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period **will** apply and **will** expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply **will**, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 9/3/2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Acknowledgement is made of Applicant's remarks and amendments filed September 3, 2009. Acknowledgement is made of Applicant's addition of a new Claim, Claim 12, in the response filed September 3, 2009. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 1 – 12 are currently pending

Priority

This application, filed 10/13/2006 is a national stage entry of PCT/GB05/50050, international filing date 04/13/2005 and claims the benefit of foreign priority to GB0408199.8, filed 04/13/2004 and GB0504501.8, filed 03/07/2005. The Claims from the instant application are supported in the specification of foreign priority document GB0408199.8, filed 04/13/2004.

Withdrawn Rejections

Claim rejections – 35 USC § 112 – 1st Paragraph

The Written Description rejection of Claims 1 – 10 under 35 U.S.C 112 1st paragraph is rendered moot and is withdrawn in response to Applicant's amendments.

Claim rejections – 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 1 – 10 under 35 U.S.C. 112, second paragraph as being indefinite is rendered moot and is withdrawn in response to Applicant's amendments.

New and/or Maintained Rejections

Claim rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Instant Claims 1 – 11 remain rejected and new claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, J.R. in US patent 6,190,701 (published: 02/20/2001) in view of Johnson, K.A. in US patent 5,376,359 (published: 12/27/1994) and Owens, J.G, in Low GWP Alternatives to HFCs and PFCs, Report of 3M Company Specialty Materials, St. Paul, MN, USA (2000).

Instant Claim 1 is drawn to a composition comprising an active ingredient preserved in a particle and suspended in a fluorinated solvent. The Roser reference teaches a composition comprising a bioactive compound and sugar glass particles (Abstract) and that such compositions are preserved or stabilized by suspension in a liquid (Column 9, Example 2). The Roser reference discloses the use of perfluorohydrocarbons as the liquid component but does not teach the use of fluorinated ether solvents as recited in amended Claim 1.

The Johnson reference teaches a composition comprising a solid particulate drug composition with a fluoropolyether that forms a stable suspension (Abstract). The Johnson reference also teaches that such compositions may comprise hydrofluoroethers (Column 2, lines 41 – 42 and 59 – 64).

Regarding instant Claim 2, the Roser reference discloses compositions comprising particles that contain sugar glass (Abstract, Claim 1).

Regarding instant Claim 3, the Roser reference discloses formulations in which additional components are added to the particles to provide a density in which the particles are stably dispersed (Column 7, lines 16 – 18; Claim 13).

Regarding instant Claim 4, the Roser reference discloses that the liquid may be blended with different components to achieve the desired density (Column 5, lines 49 – 56).

Regarding instant Claim 5, the Roser reference teaches formulations comprising a perfluorocarbon and an additional component of instant Claim 1, such as perfluorodecalin and sugar glass (Column 9, lines 20 – 22).

Regarding instant Claim 6, the Roser reference discloses a formulation comprising in which the bioactive agent is a vaccine (Column 5, lines 40 – 44; Claim 17).

Regarding instant Claims 7 – 9, drawn to a formulation in which the particles are prepared by different methods, the Roser reference disclose that the particles may be made by the conventional techniques of spray-drying, freeze-drying and milling (Column 5, lines 65 – 67; Column 6, lines 6 – 7; Example 5).

Regarding instant Claim 10, the Roser reference discloses a method in which fluorinated solvents are selected in order to provide the required density matching (Column 9, lines 20 – 27).

Regarding instant Claim 11 and newly added Claim 12, as noted in the rejection of instant Claim 1, the Johnson reference teaches a composition comprising a solid particulate drug composition in which the liquid may comprise hydrofluoroethers (Column 2, lines 41 – 42 and 59 – 64).

Thus, it would have been *prima facie* obvious to one skilled in the art, to expand upon the use of perfluorohydrocarbons, as previously taught by the Roser reference,

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and create compositions comprising more modified highly fluorinated liquid derivatives, such as fluorinated ethers related to those cited in instant Claim 1, to arrive at the claimed invention.

In addition to the teachings of Johnson, one would have been further motivated by the teachings of Owens regarding the greenhouse effect of PFCs, as cited in the prior art disclosed in the Roser reference, to seek alternative components to any PFC-based composition. In a review, Owens also notes the high global warming potential of PFCs and the need to develop alternatives. The specific selection of ether-based fluorinated compounds as a suitable liquid component of the claimed invention is further guided by the teachings of Owens who discloses hydrofluoroethers as potential alternatives to PFCs (Abstract, 3rd paragraph, Table 2). Furthermore, the Owens reference specifically discloses the HFEs 7100 and 7200 as well as the critical property of density, in Table 4.

Thus, it would have been *prima facie* obvious to one skilled in the art to combine the teachings of the Roser reference with the teachings provided by Owens and Johnson to incorporate HFEs as alternative liquid components to provide the stabilized formulations of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent

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and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 – 6 and 10 – 12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1 – 4, 13 and 16 – 18 of Roser in U.S. Patent 6,190,701, in view of Johnson in US patent 5,376,359.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons below:

As noted in the 103(a) rejections above, the prior art disclosed by Roser cited compositions comprising an active ingredient comprising a bioactive compound preserved in sugar glass particles suspended in a fluorinated solvent. The Roser reference claims the use of perfluorohydrocarbons as the liquid component but does not teach the use of ether, amine or thioether-based fluorinated solvents as described in the general formula of instant Claim 1. The Johnson reference teaches a composition comprising a solid particulate drug composition with a fluoropolyether that forms a stable suspension (Abstract). The Johnson reference also teaches that such compositions may comprise hydrofluoroethers. Thus, it would have been *prima facie* obvious to one skilled in the art, to expand upon the use of perfluorohydrocarbons, as previously taught by the Roser reference, to examine more modified highly fluorinated liquid derivatives, such as fluorinated ethers related to those cited in instant Claim 1 to arrive at the claimed invention.

Conflicting Claims 1 – 4 claim a composition cited in instant Claims 1 and 2. The conflicting claims do not teach the use of ether-based fluorinated solvents which, as noted above, is taught by the Johnson reference. Conflicting Claim 13 claims the density matching formulation regarding the particles cited in instant Claim 3 while conflicting Claim 16 discloses the formulation regarding the composition of the liquid component. Conflicting Claim 17 claims that the bioactive compound may be a vaccine, which is cited in instant Claim 6.

Response to Arguments

Applicant's arguments filed September 3, 2009 with respect to the rejection under 35 U.S.C 103(a) of Claims 1 – 11 as being unpatentable over Roser, J.R. in US patent 6,190,701 (published: 02/20/2001) in view of Johnson, K.A. in US patent 5,376,359 (published: 12/27/1994) and Owens, J.G, in Low GWP Alternatives to HFCs and PFCs, Report of 3M Company Specialty Materials, St. Paul, MN, USA (2000) have been fully considered but are not found to be persuasive.

Applicant contends that there is no teaching or suggestion within the cited references above to modify the perfluorocarbon-containing formulations of Roser to include a fluorinated ether to arrive at the present invention with improved dispersion properties (response, page 6, 3rd paragraph). Further, Applicant contends that Johnson is silent with respect to the dispersion properties of the specific fluorinated polyethers identified in column 2, lines 58 – 63).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the dispersion properties of fluorinated solvents) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Even assuming *arguendo* that the property of dispersion was a recited element in the instant Claims, it is noted that Johnson does teach favorable stabilization (dispersion or suspension) properties of particles formulated with fluoropolyethers (Examples 1 – 13). Accordingly, one of ordinary skill, cognizant of the ability of perfluoroether-containing liquid pharmaceutical compositions to stabilize (prevent flocculation or aggregation) of the particles of Johnson would have been motivated to examine compositions comprising fluoropolyethers with a reasonable expectation of success that said materials would prevent aggregation of the glassy particles of Roser.

With respect to the Owens reference, Applicant contends that while Owens teaches hydrofluoroethers, the reference does not specifically teach the beneficial dispersion properties of the present invention (response, page 6 – 7, bridging paragraph). In response, the Examiner agrees that the Owens reference does not teach the beneficial dispersion properties of hydrofluoroethers, but as noted above, the feature of dispersion is not recited in the rejected claims. It is further noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references (Roser in view of Johnson and Owens). See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Owens reference is cited as motivation to one of ordinary skill to modify the teachings of Roser and Johnson. Owens teaches that hydrofluoroethers are nonflammable and low in toxicity and, notably, are suitable alternatives to ozone depleting compounds such as perfluorinated hydrocarbons (PFC's, such as those taught by Roser, as cited in the Office Action, page

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11). Moreover, Owens specifically teaches the identical hydrofluoroethers, HFE 7100 and 7200 (Table 2, Office Action, page 11) disclosed by Applicant. Owens teaches that said hydrofluoroethers are advantageous in that they have significantly lower atmospheric lifetimes and reduced global warming potential (GWP) compared to any nonflammable commercial hydrofluorocarbon (Office Action, page 11, citing Owens Table 2, paragraph 3). Further, with respect to the limitation of Claim 1 that the particles are suspended in a liquid comprising a fluorinated ether, Owens also teaches the density of HFE-7100 (Table 4, Office Action, page 11) which is less than the PFC's of Roser (Table 1) and thus would have been expected to reduce the risk of the glassy particles of Roser from undesirable floating.

In effect, Johnson teaches that fluorinated polyethers have a beneficial effect on dispersion properties of particles and Owens teaches that fluorinated polyethers have a beneficial effect relative to perfluorohydrocarbons with respect to a lower GWP as well as a favorable density. Thus, in recognition of the benefits of the instantly claimed perfluoropolyethers one of ordinary skill would have had significant motivation to substitute the fluorinated ethers of Johnson, and particularly the hydrofluoroethers of Owens for the perfluorohydrocarbons of Roser to arrive at the instantly claimed invention with a high expectation of success

In KSR v. Teleflex, 82 USPQ2d 1385, 1397 (U.S. 2007), the Supreme Court has held that when there is market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person has good reason to pursue known options within his or her technical grasp. Under these conditions, "obviousness to try"

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such options is permissible. In this instance, a market pressure exists in the medical/pharmaceutical industries to reduce flocculation or aggregation (Johnson) or to reduce the environmental impact (Owens) of a liquid formulation comprising suspended bioactive particles. Accordingly, it would have been obvious to have examined the available fluorinated ethers taught by Johnson and Owens as they provide a solution to the technical and environmental problems cited above.

With respect to the Double Patenting rejection, Applicant contends that amendment to Claim 1 makes the rejection moot. The Examiner does not find this argument persuasive as the rejection is based on the Claims of Roser in combination with the disclosed fluorinated ethers and hydrofluoroethers of Johnson. Further, Applicant has provided no additional reasons for withdrawal of the Double Patenting rejection.

Conclusion

Claims 1 – 12 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Thursday 8AM-5PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached at (571)272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Brandon J Fetterolf/

Primary Examiner, Art Unit 1642